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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/486,069 06/07/95 ENGELHARDT

D ENZ-5 (D8) (C2)

HM12/0130

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EXAMINER

MARSCHEL, A

ART UNIT	PAPER NUMBER
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1631

56

DATE MAILED:

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No. 08/486,069	Applicant(s) Engelhardt et al.
Examiner Ardin Marschel	Group Art Unit 1631

Responsive to communication(s) filed on May 23, 2000

This action is FINAL.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle* 35 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

- Claim(s) 569-717, 719-869, 871-1021, 1023-1173, 1175-1294, 1296-1407, 1409-1568 ^(1570-1612, + 1614-1727) is/are pending in the application.
- Of the above, claim(s) _____ is/are withdrawn from consideration.
- Claim(s) _____ is/are allowed.
- Claim(s) 569-717, 719-869, 871-1021, 1023-1173, 1175-1294, and 1296-1407, 1409-1568 ^(1570-1612, + 1614-1727) is/are rejected.
- Claim(s) _____ is/are objected to.
- Claims _____ are subject to restriction or election requirement.

Application Papers

- See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- The drawing(s) filed on _____ is/are objected to by the Examiner.
- The proposed drawing correction, filed on _____ is approved disapproved.
- The specification is objected to by the Examiner.
- The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- All Some* None of the CERTIFIED copies of the priority documents have been
- received.
- received in Application No. (Series Code/Serial Number) _____.
- received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
- *Certified copies not received: _____
- Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- Notice of References Cited, PTO-892
- Information Disclosure Statement(s), PTO-1449, ~~Page 1 of 13~~ (13 sheets)
- Interview Summary, PTO-413
- Notice of Draftsperson's Patent Drawing Review, PTO-948
- Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

Applicants' arguments and amendments; filed 5/23/00, 6/20/00, 8/30/00, 8/31/00, 9/8/00, and 11/16/00; have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. They constitute the complete set presently being applied to the instant application.

Claims 569-717, 719-869, 871-1021, 1023-1173, 1175-1294, 1296-1407, 1409-1568, 1570-1612, and 1614-1727 are rejected, as discussed below, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is noted that the instant disclosure is directed to the preparation and use of nucleotide analogs wherein they are labeled or modified in their chemical structure so as to be non-radioactively detectable. Radioactive analogs are also described, especially in the reference which is incorporated by reference to Ward et al. (P/N 4,711,955) wherein radioactive elements are present in prior art labeled nucleic acids. The replacement of such radioactive nucleotide labels with non-radioactive alternatives is extensively summarized in columns 1-3. Numerous biotinylated nucleotides and corresponding nucleic acid polymers are described in said Ward et al. as well as in the instant application wherein numerous nucleotide analogs and

polynucleotides are described. Consideration of the entirety of these two disclosures, however has failed to reveal preparatory or use descriptions for the inventions therein described wherein the labeling includes both radioactive and non-radioactive means, except for a specific set of embodiments directed to chelating a radioactive metal. It is noted that even the chelating groups per se are non-radioactive. Only the metal gives radioactivity to the label. Metals are listed in the instant specification as filed on page 85. No other radioactive labeling is described as to its preparation or use in the instant disclosure. It is noted that all of the independent claims that are presently pending fail to limit the invention to non-radioactively labeled nucleotide practice and thus the claims are not commensurate in scope with the specification, especially because double modification is only disclosed in the radioactive metal-chelator embodiments. For example, in claim 569, lines 3-11, the nucleic acid fragments therein are detectable and labeled and are optionally described as modified or as analogs. Then in the last three lines of claim 569 they are detected non-radioactively. Thus, these two sections of the claim differ in scope in that the lines 3-11 are inclusive of a wide variety of labeled or modified nucleotide practice whereas in contrast only non-radioactive detection is performed in the last 3 lines. It is noted that radioactive detection is disclosed wherein chelated radioactive

metal is present in the nucleic acid probe. Thus unclarity pertains to claims 569-717, 719-869, 871-1021, 1023-1173, 1175-1294, 1296-1407, 1409-1568, 1570-1612, 1614-1699, and 1712-1727. Clarification is requested via clearer claim wording.

Claims 1700-1711 are vague and indefinite for a similar reason as the above claims. In these claims chelating nucleotide analogs are described but without clarifying the radioactive presence as being in the metal that is chelated. For example, in claim 1700, lines 3-13, chelating compounds or components are described but without indicating the presence or absence of a radioactive metal. It is noted that chelating compounds or components do not necessarily actually contain a chelated metal. They may be and usually are prepared without the metal presence which is only added later during a radioactive labeling step. Clarification via clearer claim wording is requested in order to clearly word the claims to correspond to the chelating-metal practice in the specification.

Claims 1712-1718 and 1727 are additionally vague and indefinite in that these claims are directed to detecting a nucleic acid of interest but do not contain any specificity of hybridization. Also, the last line of the claim lacks any indication that the resolved hybrids only contain the nucleic acid of interest hybridized to the labeled oligonucleotide or polynucleotide as an indication of detecting the presence of the

nucleic acid of interest. Clarification is requested via clearer claim wording as to some type of specificity which results in actual nucleic acid of interest detection.

Claim 602 is vague and indefinite in that moieties y and z are indicated as either being H- or HO- whereas claim 602 also indicates open claim language via the word "comprise" in line 2. It is unclear what additionally would be present in y or z to correspond to the open word "comprise". Claims 754, 906, and 1058 also contain this unclarity.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1298-1302, 1304, 1306, 1320, 1327-1333, 1336-1340, 1342, 1343, 1345-1350, 1352, 1353, 1355, 1358-1360, 1371, 1373, 1374, 1385, 1386, 1388-1394, 1396, 1398-1400, 1403, 1404, 1406, 1407, 1409, 1410, 1582, 1583, 1601, 1612, 1614-1618, 1622, 1627-1639, 1641, 1642, 1644-1648, 1650, 1651, 1653, 1656-1658, 1662, 1669, 1671, 1672, 1677, 1682, 1684, 1686-1690, 1692, 1694-1699, 1705, 1711, and 1725 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Broker et al. (NAR 5:363[1978]).

Broker et al. discloses the incorporation of biotin onto a

3' terminus of a tRNA via a diamino alkyl bridge as summarized in the abstract which is then utilized to hybridize to phage DNA. The hybrid is visualized in Figure 5 on page 377 in a non-radioactive manner via ferritin. The 3' terminal labeling may be viewed either as sugar moiety labeling or phosphate moiety labeling of the penultimate nucleotide in the tRNA. It is additionally noted that the incorporation of this label is performed in the EXPERIMENTAL PROCEDURES via 3' modification of the tRNA and thus incorporated in parts. The instant claims, however, do not limit the manner of incorporation thus supporting the anticipation of the instant claims as listed above.

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103,

the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1712-1718 and 1727 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Langer et al. (PNAS 78:6633[1981]) taken in view of Axel et al. (P/N 4,399,216).

Langer et al. describes the practice of biotin labeling of hybridization probes therein, taken as a whole. Langer et al. suggests and motivates various uses of such non-radioactively labeled probes including in blots in the DISCUSSION section on page 6637. Langer et al. lacks specifics as to blot hybridization practice.

Axel et al. contains a description of a famous type of blot, called a Southern blot in column 19, line 44, through column 20, line 15, wherein agarose gel electrophoresis is utilized to separate nucleic acids by size with detection in this case by radioactive labeling.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to have substituted the biotin non-radioactive labeling of Langer et al. in the Axel et al. Southern blot procedure as motivated by Langer et al. for such substitution with a reasonable expectation of success as given in Langer et al. thus resulting in the instant

invention practice. It is noted that instant claim 1298 is not limited as to what chemical non-radioactive structure is being practiced therein.

The disclosure is objected to because of the following informalities:

In claims 1725 and 1726 the word "direction" appears to be misspelled in context.

Appropriate correction is required.

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703)305-3014 or (703)308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703)308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703)308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, Tina Plunkett, whose telephone number is (703)305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

January 26, 2001

Ardin H. Marschel
ARDIN H. MARSCHEL
PRIMARY EXAMINER